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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,388	02/05/2004	Horst Georg Zerbe	2004-0189	3058

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EXAMINER	
ROBERTS, LEZAH	
ART UNIT	**PAPER NUMBER**
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/771,388	ZERBE ET AL.	
	Examiner	Art Unit	
	Lezah W. Roberts	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *October 16, 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-51* is/are pending in the application.

4a) Of the above claim(s) *41-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the Amendment filed October 16, 2006. All previous rejections have been withdrawn unless stated below.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims

Claim Rejections - 35 USC § 101/35 USC § 112 - Product/Process (New Rejection)

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10-23 are rejected under 35 U.S.C. 101, which fails to set forth the statutory class of the invention. The claims recite "said film effects the transmucosal delivery of said one or more pharmaceutically active agents when adhered to the said oral cavity". The claims embrace both product and process of using, which violates the rule an invention should set forth the statutory class of invention in the alternative form.

Claims 10-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim purports to be both a product and a

process, which makes it ambiguous and therefore does not particularly point out and distinctly claim the metes and bounds the invention.

See Ex parte Lyell 17 USPQ2d 1548.

Claim Rejections - 35 USC § 112 – New Matter (New Rejection)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims recite the limitation "said film effects the transmucosal delivery". There appears to be no support for this limitation. Applicant appears to have support for delivering the compositions to the mucosa but not necessarily across the mucosal membrane.

Claim Rejections - 35 USC § 103 – Obviousness (Previous Rejections)

1) Claims 10 and 13 were rejected under 35 U.S.C. 103(a) as being unpatentable over Schmidt (US 5,354,551). The rejection is maintained.

Applicant amends the claims by adding the limitation "said film effects the transmucosal delivery of said one or more pharmaceutically active agents when

adhered to the oral cavity". Applicant argues because the preparation is used similarly to toothpaste, mucoadhesiveness would interfere with its intended use. The mucoadhesiveness would cause the preparation to stick to the oral mucosa. The antibacterial agents are added to provide local antibacterial action exclusively in the oral cavity, without being absorbed by the oral mucosa. Schmidt does not indicate that the mouth and tooth care preparations are suitable for effecting transmucosal delivery of the "antibacterial agents". This argument is not persuasive.

"Mucoadhesiveness" simply means adheres to mucosa. The films of the reference dissolve to form toothpastes. Toothpastes are in fact used to deliver substances through the oral mucosa[1] and therefore having mucoadhesive polymers in toothpaste are advantageous. Applicant is reciting a composition, which is encompassed by the reference, such that intended use carries no weight in determining the patentability of the compositions because the compositions of the reference and the compositions of the instant claims are substantially the same. Accordingly, the act of delivering pharmaceutically active agents by transmucosal delivery is intended use.

2) Claim 19 was rejected under 35 U.S.C. 103(a) as being unpatentable over Schmidt (US 5,354,551) in view of Story et al. (US 4,944,949). The rejection is maintained.

Applicant's arguments for Schmidt are discussed above. Story et al. critically depends on the presence of a particular type of drug and surfactants that are capable of

[1] Specht, German Patent 19,615,820, page3, paragraph 3, October 1997

forming micelles when combined with these particular drug substances. The surfactant is not merely used "to dissolve the drug" but is used in order to allow micelle formation. Furthermore Schmidt does not refer to NSAIDS and it is not known whether the "additives" in Schmidt would be suitable for micelle formation. Schmidt discloses the tensides are used as foaming agents. The arguments are not persuasive.

See arguments above in regards to Schmidt. Story et al. is used as a general reference to show the benefits of using two or more surfactants when a pharmaceutically active agent is present. Schmidt suggests the use of more than one surfactant and Story et al. discloses the benefits of using one or more surfactants, therefore giving motivation to combine the two references. Although Schmidt does not refer to NSAIDs in its disclosure it does mention additives and Applicants' instant claims do not recite the type of pharmaceutically active agent present in the instantly claimed compositions. Therefore the rejection stands.

3) Claims 11-12, 14-18 and 21-23 were rejected under 35 U.S.C. 103(a) as being unpatentable over Schmidt (US 5,354,551) as applied to claims 10 and 13 above, and further in view of Acharya (US 5,686,094). The rejection is maintained.

Applicant's arguments for Schmidt are discussed above. Applicant argues Acharya disclosed mouth and tooth care products (that are intended for hygienic purposes but rather for therapeutic purposes) but relates to drug delivery systems. Therefore the combination of the references would not be obvious. The argument is not persuasive.

It would have been obvious to one of ordinary skill in the art to have looked to Acharya, which teaches oral films, in order to improve the aesthetics of the toothpaste films to make the films pleasing to the consumer. Further more Archarya disclose delivering fluoride with the films, which is also a function of Schmidt. Regarding transmucosal delivery, mucoadhesion is inherent and delivery across the mucosa is merely an intended use, as previously discussed.

4) Claims 24-27 and 32 were rejected under 35 U.S.C. 103(a) as being unpatentable over Keith et al. (US 4,764,378) in view of Acharya (US 5,686,094). The rejection is maintained in regards to claims 24-27 and withdrawn in regards to claim 32.

Applicant argues the additional ingredients that may be added to the compositions of Keith et al. are not specified and are added to modify the physical properties of the matrix. Keith provides no motivation for adding ingredients that add function. Acharya does not mention nicotine as an active substance. Applicant further points out that nicotine is a substance having an unpleasant odor and a sharp, burning taste. Therefore, there would be no reason to combine the references. These arguments are not persuasive.

Keith et al. disclose, "Additional ingredients in minor amounts may be incorporated into the buccal matrix of the invention to provide desirable physical properties or modify the properties of the matrix" (col. 4, lines 28-33). This may include properties such as taste because taste is a property of the matrix. The reference also discloses polyvinylpyrrolidone acts as an odor masking substance. Acharya includes

breath fresheners and flavorants. Therefore it would have been obvious to one of ordinary skill in the art to have used breath fresheners or flavorants from the drug delivery films of Acharya in the films of Keith et al. to mask odor.

5) Claims 20 and 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keith et al. (US 4,764,378) in view of Story et al. (US 4,944,949). The rejection is maintained in regards to claim 20 and withdrawn in regards to claims 36-37.

Applicant argues Keith et al., merely mentions the possibility of adding additional ingredients for modifying the physical properties of the matrix, but do not teach incorporating surfactants. Story et al. does not mention nicotine only NSAIDs. In regards to Keith et al. [It is believed Applicant means Story et al., since the addition of surfactants according to Keith et al. is mentioned specifically in connection with micelle formation in the presence of NSAIDs, it is apparent that one skilled in the art would not have used the surfactants and mixtures thereof disclosed by Story et al. in the buccal dosage forms taught by Keith et al. This argument is not persuasive.

As mentioned above Story et al. is a general teaching disclosing the advantages of using more than one surfactant as well as surfactants used to deliver pharmaceutically active agent. See answer to Applicant's argument in subsection 2.

Claim Rejections - 35 USC § 103 – Obviousness (New Rejection)

1) Claims 28-29, 31, 33-35, and 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keith et al. (US 4,764,378) in view of Inoue et al. (US 4,772,470).

Keith et al. teach dosage forms for administration of drugs and more particularly buccal dosage forms having a polymeric matrix for controlled release of a drug. The composition comprises three essential ingredients: from about 20% to about 75% by weight of a low molecular weight polyethylene glycol component, from about 2% to about 65% by weight of a medium or high molecular weight polyethylene glycol component, and from about 1% to about 40% by weight of an auxiliary high molecular weight polymer. The dosage forms include disks, wafers, tablets, lozenges, lamellae and the like. Suitable high molecular weight polymers include polyvinylpyrrolidone (PVP), polyethylene oxide (PEO), poly(acrylic acid) (PAA), sodium alginate and carboxymethyl cellulose, which encompasses claim 31. Preferred high molecular weight polymers include polyvinyl pyrrolidone and polyethylene oxide. Both of these polymers provide the matrix with water-activated adhesive properties for good adhesion to the oral mucosa. The polymers are incorporated into the compositions at concentrations ranging fro about 25% to about 40% encompassing claim 33. The dosage form rapidly disintegrates and dissolves after being placed in the mouth, encompassing the instant claims (col. 4, lines 1-20). Additional ingredients may be incorporated into the buccal matrix of the invention to provide desirable physical properties or modify the properties of the matrix (col. 4, lines 28-33), encompassing

claims 34-35. For example, a plasticizer such as propylene glycol may be added in amounts up to about 5% by weight of the matrix. Preferred drugs for incorporation into the buccal dosage form include nicotine (col. 5, line 30). The active ingredient will generally comprise from about 0.01 percent by weight to about 10 percent by weight of the dosage form (col. 5, lines 40-44), encompassing claim 38. Suitable dimensions for the dosage form are a length of 5 to 10 mm, a width of 2 to 10 mm and a thickness of 0.2 to 3 mm (col. 6, lines 1-9), encompassing claim 29. Lamellae dosage forms with a certain composition dissolved rapidly when placed in the buccal pouch or sublingually (col. 6, lines 33-35). A small amount of a dye may also be incorporated into the matrix.

The reference differs from the instant claims insofar as it does not disclose the thickness of the films to be no more than 70 μm and does not disclose flavorings.

Inoue et al. discloses oral bandages and oral preparations. The preparations comprise an adhesive film comprising a drug. The thickness of the resulting film is preferably adjusted to a range of from 5 to 100 micrometers by controlling the amount of the casting solution, and the like. If a film thickness is less than 5 micrometers it is difficult to obtain sufficient adhesion. A film having a thickness exceeding 100 micrometers tends to produce a feeling foreign to the mouth and to impair softness of the film. Other additives are added to the compositions such as flavoring and coloring matter. The reference differs from the instant claims insofar as it does not disclose nicotine in the compositions.

It would have been obvious to one of ordinary skill in the art to have adjusted the thickness parameters of between 5 to 100 micrometers of the films of the primary

reference motivated by the desire to obtain sufficient adhesion while not producing a film that has a foreign feeling in the mouth, as disclosed by the secondary reference. (Note that this is the same reason preferred by Applicant. See Remarks, page 11, lines 5-6 from the bottom.)

2) Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Keith et al. (US 4,764,378) in view of Inoue et al. (US 4,772,470) as applied to claims 28-29, 31, 33-35, and 38-40 above, and further in view of Stanley et al. (US 5,783,207).

The primary and secondary references are discussed above. The disclosures of the combined references differ from the instant claims insofar as they do not disclose incorporating nicotine salts into the film compositions.

Stanley et al. teach dosage forms comprising nicotine and its salts. Nicotine is released from a dosage form and absorbed through the intra-oral mucosal surfaces as the nicotine-containing matrix releases nicotine within the user's mouth. Nicotine is available in either the free base or salt form. Nicotine base is readily absorbed through mucosal membranes but is highly volatile. Nicotine salts, on the other hand, are not readily absorbable through mucosal membranes but are much more stable. Pharmaceutically acceptable nicotine salts include, but are not limited to nicotine hydrochloride and nicotine salicylate. In an alkaline environment, i.e., pH above about 7, and in the presence of an aqueous medium, such as saliva within the oral cavity, nicotine salts react to form nicotine base (col. 7, lines 38-60). In addition to nicotine in a releasable form, which is readily absorbed transmucosally; the nicotine-

containing compositions in accord with the present invention may contain other ingredients such as flavorings, sweeteners, flavor enhancers, lubricants, binders and fillers.

The reference differs from the instant claims insofar as it does not disclose the matrices as being able to rapidly disintegrate or soften immediately.

It would have been obvious to one of ordinary skill in the art to have used the nicotine salts and other ingredients in the compositions of the combined primary and secondary reference motivated by the desire to produce a dosage form wherein the nicotine active ingredient is more stable (less volatile) than the nicotine base and then forms the nicotine base when introduced into the oral cavity when in the presence of saliva, as disclosed by the tertiary reference.

3) Claims 36-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keith et al. (US 4,764,378) in view of Inoue et al. (US 4,772,470) as applied to claims 28-29, 31, 33-35, and 38-40 above, and further in view of Story et al. (US 4,944,949).

The primary and secondary references are discussed above. The reference differs from the instant claims insofar as it does not disclose incorporating surfactants into the oral compositions.

Story et al. teach pharmaceutical delivery systems comprising drugs formulated with surfactants (see abstract). The surfactant is used to dissolve the drug. Surfactants can be variously classified, and often by reference to the nature of the hydrophilic region, which can be anionic, cationic, zwitterionic or nonionic. The preferred

surfactants of the reference are nonionic surfactants, which include polyoxyethylated surfactants, including polyoxyethylated glycol monoethers, polyoxyethylated fatty acids, polyoxyethylated sorbitan fatty esters, and polyoxyethylated castor oils. However, other nonionic surfactants are also particularly appropriate, including sorbitan fatty acid esters, poloxamers, polyethylene glycol fatty acid esters and polyethoxylated glyceryl fatty acid esters. Whatever the precise chemical structure of the surfactant or surfactants used, it is generally preferred to use one or more of those that have been already cleared for human ingestion. Therefore, surfactants with a low toxicity are preferred. One factor affecting the choice of surfactant or surfactants to be used is the hydrophilic-lipophilic balance (HLB), which gives a numerical indication of the relative affinity of the surfactant for aqueous and non-aqueous systems. There may be cases where a mixture of two or more surfactants provides an improved degree of solubilization over either surfactant used alone. Additional components may be added to the compositions such as preservatives, sweeteners and flavoring agents.

The reference differs from the instant claims insofar as it does not disclose the oral compositions as a monolayer film or the oral compositions comprising water-soluble polymers comprising nicotine.

It would have been obvious to one of ordinary skill in the art to have used the surfactants and mixtures thereof in the compositions of the primary reference motivated by the desire to ensure a uniform mixture throughout the film thoroughly dissolve the drug being incorporated into the film as taught by the secondary reference.

Claims 10-40 are rejected.

No claims allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lezah W. Roberts whose telephone number is 571-272-1071. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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